# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 22 | CLEAVAGE ADJ5 NOTCH AND @AD<="19980723" | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | AND | ON | 2007/05/19 15:52 |
| L2 | 44 | Activation ADJ5 NOTCH AND @AD<="19980723" | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | AND | ON | 2007/05/19 15:52 |
| L3 | 5 | Modulation AND L1 | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | AND | ON | 2007/05/19 15:53 |
| S1 | 4 | 09/121457 | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | AND | ON | 2006/10/23 13:52 |
| S2 | 5 | "6436650" | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT | AND | ON | 2006/10/23 13:57 |

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TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 08   CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  3  JAN 16   CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS  4  JAN 16   IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16   WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22   CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22   CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29   PHAR reloaded with new search and display fields
 NEWS  9  JAN 29   CAS Registry Number crossover limit increased to 300,000 in
                   multiple databases
 NEWS 10  FEB 15   PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15   RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23   KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26   MEDLINE reloaded with enhancements
 NEWS 14  FEB 26   EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26   TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26   IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26   CAS Registry Number crossover limit increased from 10,000
                   to 300,000 in multiple databases
 NEWS 18  MAR 15   WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16   CASREACT coverage extended
 NEWS 20  MAR 20   MARPAT now updated daily
 NEWS 21  MAR 22   LWPI reloaded
 NEWS 22  MAR 30   RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02   JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30   GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30   CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30   CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30   INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01   New CAS web site launched
 NEWS 29  MAY 08   CA/CAplus Indian patent publication number format defined
 NEWS 30  MAY 14   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 10:03:08 ON 19 MAY 2007

=> File .Gerry1
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'BIOSIS' ENTERED AT 10:03:20 ON 19 MAY 2007
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FILE 'CAPLUS' ENTERED AT 10:03:20 ON 19 MAY 2007
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FILE 'MEDLINE' ENTERED AT 10:03:20 ON 19 MAY 2007

=> S Activation(5A)Notch AND pd<=20040217
   3 FILES SEARCHED...
L1         1274 ACTIVATION(5A) NOTCH AND PD<=20040217

=> Dup rem l1
PROCESSING COMPLETED FOR L1
L2          503 DUP REM L1 (771 DUPLICATES REMOVED)

=> S Cleavage(5A)Notch AND pd<=20040217
L3          524 CLEAVAGE(5A) NOTCH AND PD<=20040217

=> Dup Rem L3
PROCESSING COMPLETED FOR L3
L4          253 DUP REM L3 (271 DUPLICATES REMOVED)

=> S Modulation(S)(Cleavage(5A)Notch) AND pd<=20040217
L5            6 MODULATION(S)(CLEAVAGE(5A) NOTCH) AND PD<=20040217

=> Dup Rem L5
PROCESSING COMPLETED FOR L5
L6            3 DUP REM L5 (3 DUPLICATES REMOVED)

=> D Ibib Abs L6 1-3

L6   ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
     DUPLICATE 1
ACCESSION NUMBER:   2003:466485  BIOSIS
DOCUMENT NUMBER:    PREV200300466485
TITLE:              Abeta42-lowering nonsteroidal anti-inflammatory drugs
                    preserve intramembrane cleavage of the amyloid precursor
                    protein (APP) and ErbB-4 receptor and signaling through the
                    APP intracellular domain.
AUTHOR(S):          Weggen, Sascha [Reprint Author]; Eriksen, Jason L.; Sagi,
                    Sarah A.; Pietrzik, Claus U.; Golde, Todd. E.; Koo, Edward
                    H.
CORPORATE SOURCE:   Department of Neurosciences, University of California San
                    Diego, La Jolla, CA, 92093, USA
                    sweggen@ucsd.edu
SOURCE:             Journal of Biological Chemistry, (August 15 2003)
                    Vol. 278, No. 33, pp. 30748-30754. print.
                    CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE:      Article
```

LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003

AB Epidemiological studies indicate that long term use of nonsteroidal anti-inflammatory drugs (NSAIDs) confers protection from Alzheimer's disease, and some NSAIDs were shown to specifically decrease production of the amyloidogenic Abeta42 peptide, most likely by direct modulation of gamma-secretase activity. In contrast to) gamma-secretase inhibitors, Abeta42-lowering NSAIDs do not impair S3 cleavage in the NOTCH receptor and release of the NOTCH intracellular domain, a finding with conceptual implications for the development of safer drugs targeting Abeta production through gamma-secretase modulation. Intramembrane cleavage and release of an intracellular signaling domain has recently been demonstrated in a number of additional gamma-secretase substrates. We now show in cell-based assays that intramembrane cleavage of APP and ErbB-4 receptor is not impaired by the Abeta42-lowering NSAIDs, sulindac sulfide and ibuprofen. Generation of the APP intracellular domain (AICD) was further not inhibited in a cell-free assay at concentrations far exceeding those effective in reducing Abeta42 production. Closer inspection of AICD signaling showed that stabilization of the AICD peptide by FE65 and AICD-mediated transcription were also retained at Abeta42-lowering concentrations. These results demonstrate that S3-like/intramembrane cleavage is preserved by Abeta42-lowering NSAIDs in at least three substrates of gamma-secretase APP, ErbB-4, and NOTCH and underline the striking specificity by which these drugs target Abeta42 production.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:123354 CAPLUS
DOCUMENT NUMBER: 136:182442
TITLE: Assay
INVENTOR(S): Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman, Margaret Jane; Champion, Brian Robert
PATENT ASSIGNEE(S): Lorantis Limited, UK
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002012890 | A2 | 20020214 | WO 2001-GB3503 | 20010803 <-- |
| WO 2002012890 | A3 | 20030313 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001076499 | A5 | 20020218 | AU 2001-76499 | 20010803 <-- |
| EP 1309859 | A2 | 20030514 | EP 2001-954152 | 20010803 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004005631 | A1 | 20040108 | US 2003-357321 | 20030203 <-- |

| PRIORITY APPLN. INFO.: | | | |
|---|---|---|---|
| GB 2000-19242 | A | 20000804 | |
| WO 2001-GB3503 | W | 20010803 | |

AB A method for monitoring the immune system comprising monitoring the Notch signaling pathway. Also, methods to assess the reactivity of T-cells to a given antigen and immune tolerance are provided. The invention further relates to a screening assay for modulators of Notch signaling and to

modulators identifiable by such an assay. Detecting modulation of Notch signaling will comprise a step of detecting cleavage of the intracellular domain of Notch; detecting interaction of Suppressor of Hairless with Notch; detecting interaction of Deltex with Notch or Grb2; detecting modulation of the Ras JnK signaling pathway; or detecting cleavage of the extracellular domain of Delta.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:53664 CAPLUS
DOCUMENT NUMBER: 132:104440
TITLE: Delta protein cleavage products from the action of Kuzbanian and their biological activity and therapeutic uses
INVENTOR(S): Artavanis-Tsakonas, Spyridon; Rand, Matthew D.; Qi, Huilin
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2000002897 | A2 | 20000120 | WO 1999-US15817 | | 19990713 <-- |
| WO 2000002897 | A3 | 20000316 | | | |
| W: AU, CA, JP | | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| CA 2333893 | A1 | 20000120 | CA 1999-2333893 | | 19990713 <-- |
| AU 9950994 | A | 20000201 | AU 1999-50994 | | 19990713 <-- |
| EP 1096946 | A2 | 20010509 | EP 1999-935534 | | 19990713 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | | |
| AU 2004200166 | A1 | 20040212 | AU 2004-200166 | | 20040115 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-92513P | P | 19980713 |
| | | | US 1998-104834P | P | 19981019 |
| | | | AU 1999-50994 | A3 | 19990713 |
| | | | WO 1999-US15817 | W | 19990713 |

AB The present invention(s) are based on the discovery that the toporythmic Delta protein is cleaved by the metalloprotease-disintegrin Kuzbanian (Kuz) into 2 fragments, a soluble N-terminal fragment consisting essentially of the extracellular domain, and a membrane-bound fragment consisting essentially of the transmembrane domain and the intracellular domain. The soluble fragment of Delta, like the full-length, membrane-bound Delta, is able to bind to Notch protein, and is believed to be the actual ligand for Notch in vivo. Thus, the present invention is directed to a Delta cleavage peptide and fragments, derivative and analogs thereof, and its encoding nucleic acids, as well as to protein complexes of Delta and Kuz. Methods for detecting or measuring either Delta or Kuz activation by observing or measuring Delta cleavage products that are indicative of Delta activation are provided. Further, methods for detecting a mol. that modulates Delta activation or Kuz function by observing or measuring a change in the amount of or pattern of Delta cleavage products are also provided.

=> D Hist

(FILE 'HOME' ENTERED AT 10:03:08 ON 19 MAY 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 10:03:20 ON 19 MAY 2007
L1 1274 S ACTIVATION(5A)NOTCH AND PD<=20040217
L2 503 DUP REM L1 (771 DUPLICATES REMOVED)

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L3          524 S CLEAVAGE(5A)NOTCH AND PD<=20040217
L4          253 DUP REM L3 (271 DUPLICATES REMOVED)
L5            6 S MODULATION(S)(CLEAVAGE(5A)NOTCH) AND PD<=20040217
L6            3 DUP REM L5 (3 DUPLICATES REMOVED)

=> S L2 AND L4
L7          29 L2 AND L4

=> D Ti l7

L7   ANSWER 1 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Notch ligands differentially regulate T cell activation
     .


=> D ti L7 !-29
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'1-29' IS NOT A VALID FORMAT
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individual files.
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'D' IS NOT A VALID FORMAT
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individual files.
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L7   ANSWER 1 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Notch ligands differentially regulate T cell activation
     .


=> D Ti L7 2-29

L7   ANSWER 2 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Presenilin/Notch signals influence thymocyte differentiation, with
     distinct effects on alpha beta and gamma delta T cell development.

L7   ANSWER 3 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   The potency of inhibiting Notch - cleavage is
     increased in cells stably or constitutively expressing Notch versus
     transiently expressing Notch.

L7   ANSWER 4 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Modulation of Notch signaling by metabotropic glutamate receptors.

L7   ANSWER 5 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Osteoblasts participate in the stem cell niche regulating stem cell
     numbers by Jagged1 activation of Notch.

L7   ANSWER 6 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Activated forms of notch and methods based thereon.

L7   ANSWER 7 OF 29  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Inhibition of vascular endothelium by the Notch-ligand delta-4 unveils a
     novel therapeutic target.
```

L7 ANSWER 8 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Mind bomb is a ubiquitin ligase that is essential for efficient activation of Notch signaling by Delta.

L7 ANSWER 9 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Alleles at the Nicastrin locus modify presenilin 1-deficiency phenotype.

L7 ANSWER 10 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Activated forms of notch and methods based thereon.

L7 ANSWER 11 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Numb suppresses the negative complementation at the Notch locus of Drosophila melanogaster, suggesting a putative mechanism for negative complementation.

L7 ANSWER 12 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Novel Notch alleles reveal a Deltex-dependent pathway repressing neural fate.

L7 ANSWER 13 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Implication of APP secretases in Notch signaling.

L7 ANSWER 14 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI GSK3beta phosphorylates Notch and modulates signaling.

L7 ANSWER 15 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Deregulation of NOTCH2 signalling in B-CLL.

L7 ANSWER 16 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Notch-1 activation by familial Alzheimer's disease (FAD)-linked mutant forms of presenilin-1.

L7 ANSWER 17 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Calcium depletion dissociates and activates heterodimeric notch receptors.

L7 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Notch signaling pathway and its regulation

L7 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Notch subunit heterodimerization and prevention of ligand-independent proteolytic activation depend, respectively, on a novel domain and the LNR repeats

L7 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Distinct roles of EGF repeats for the Notch signaling system

L7 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Monoubiquitination and endocytosis direct γ-secretase cleavage of activated Notch receptor

L7 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI A novel proteolytic cleavage involved in Notch signaling: the role of the disintegrin-metalloprotease TACE

L7 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI A ligand-induced extracellular cleavage regulates γ-secretase-like

proteolytic activation of notch1

L7 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Neoplastic transformation by Notch is independent of transcriptional activation by RBP-J signaling

L7 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Activated forms of Notch and methods for detecting modulators of Notch signal transduction

L7 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI Ligand-induced cleavage and regulation of nuclear entry of Notch in Drosophila melanogaster embryos

L7 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
TI A study of the brittle fracture characteristics of CoSi2 using laser beam reflections

L7 ANSWER 28 OF 29 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Presenilin suppresses the negative complementation at the Notch locus of Drosophila melanogaster, suggesting a mechanism for negative complementation.

L7 ANSWER 29 OF 29 MEDLINE on STN
TI RIPping notch apart: a new role for endocytosis in signal transduction?.

=> S L7 AND pd<=19980723
L8 2 L7 AND PD<=19980723

=> D Ibib Abs L8 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:10383 CAPLUS
DOCUMENT NUMBER: 130:180153
TITLE: Ligand-induced cleavage and regulation of nuclear entry of Notch in Drosophila melanogaster embryos
AUTHOR(S): Kidd, Simon; Lieber, Toby; Young, Michael W.
CORPORATE SOURCE: Lab. Genetics, The Rockefeller University, New York, NY, 10021-6399, USA
SOURCE: Genes & Development (1998), 12(23), 3728-3740
CODEN: GEDEEP; ISSN: 0890-9369
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Notch, a transmembrane protein found in a wide range of organisms, is a component of a pathway that mediates cell-fate decisions that involve intercellular communication. In this paper, the authors show that in Drosophila melanogaster, Notch (N) is processed in a ligand-dependent fashion to generate phosphorylated, soluble intracellular derivs. Suppressor of Hairless [Su(H)] is predominantly associated with soluble intracellular N. It has been demonstrated by others that N has access to the nucleus, and when tethered directly to DNA, the cytoplasmic domain of N can activate transcription. Conversely, a viral activator fused to Su(H) can substitute for at least some N functions during embryogenesis. The authors suggest that one function of soluble forms of N is to bind to Su(H), and in the nucleus, to act directly as a transcriptional transactivator of the latter protein. Although N has functional nuclear localization signals, the N/Su(H) complex accumulates in the cytoplasm and on membranes suggesting that its nuclear entry is regulated. Localization studies in cultured cells and embryos suggest that Su(H) plays a role in this regulation, with the relative levels of Delta, N and Su(H) determining whether a

N/Su(H) complex enters the nucleus.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:582365 CAPLUS
DOCUMENT NUMBER: 122:320112
TITLE: A study of the brittle fracture characteristics of CoSi2 using laser beam reflections
AUTHOR(S): Anongba, P. N. B.; Oberli, S.; Steinemann, S. G.
CORPORATE SOURCE: Inst. Phys. Experimentale, Univ. Lausanne, Lausanne, CH-1015, Switz.
SOURCE: Acta Metallurgica et Materialia (1995), 43(6), 2275-85
CODEN: AMATEB; ISSN: 0956-7151
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The room temperature brittle fracture characteristics of oriented CoSi2 single crystals with edge notches, subjected to three-point bending expts., have been investigated. A rather uncommon but powerful method has been used: fractured surfaces reflect incident laser beams; the reflected beam pictures correspond to distributions of local surface normals that allow surface elements to be readily characterized. CoSi2 specimens fail according to two distinct mechanisms. The first one corresponds to the fracture of the specimen parallel to a unique crystallog. plane (the notch plane approx.). The directions of fracture propagation are always different from <110>. Various cleavage planes are associated with it such as (101), (111) and some other planes with higher indexes close to (212) and (412). The second mechanism corresponds to the simultaneous activation (about the notch) of various non-parallel local cleavage planes [such as (101), (212), (111) ...] which have the [10.hivin.1] zone axis that corresponds to the direction of fracture propagation. The local cleavage planes have normals located in the (10.hivin.1) plane between [111]-[101] or [101]-[1.hivin.11] or both.

=> S L4 AND pd<=19980723
L9 44 L4 AND PD<=19980723

=> D Ti l9 1-44

L9 ANSWER 1 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI The Notch1 receptor is cleaved constitutively by a furin-like convertase.

L9 ANSWER 2 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Indirect evidence for delta-dependent intracellular processing of notch in Drosophila embryos.

L9 ANSWER 3 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Metalloprotease-disintegrins: Links to cell adhesion and cleavage of TNF-alpha and Notch.

L9 ANSWER 4 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Intracellular cleavage of notch leads to a heterodimeric receptor on the plasma membrane.

L9 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Ligand-induced cleavage and regulation of nuclear entry of Notch in Drosophila melanogaster embryos

L9 ANSWER 6 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cleavage fracture criterion of low alloy steel and weld metal in notched specimens

L9 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Caspase-mediated cleavage is not required for the activity of presenilins in amyloidogenesis and NOTCH signaling

L9 ANSWER 8 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Large-scale simulations of brittle and ductile failure in face centered cubic crystals

L9 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Kuz family of metalloproteases involved in Notch cleavage and neurogenesis

L9 ANSWER 10 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Developmental signaling: notch signals Kuz it's cleaved

L9 ANSWER 11 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effect of long-time annealing on embrittlement of 15Cr2NiMoV steels

L9 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Anisotropy of cleavage fracture stress in thermomechanically processed microalloyed steel plate

L9 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI A study of the brittle fracture characteristics of CoSi2 using laser beam reflections

L9 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Determination of cleavage planes and fracture characterization of Ni-base single crystal superalloys

L9 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effect of notch root radius on the cleavage fracture stress σf*.

L9 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Critical assessment of the local cleavage stress σf* in notch specimens of carbon-manganese steel

L9 ANSWER 17 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cleavage fracture in B2 aluminides

L9 ANSWER 18 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Microstructural features controlling ductile-to-brittle transition behavior in high-strength, martensitic steel weld metals

L9 ANSWER 19 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cleavage fracture origins under static and dynamic loading

L9 ANSWER 20 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Fracture of single crystals of the nickel-base superalloy PWA 1480E in hydrogen at 22 °C

L9 ANSWER 21 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Hydrogen-induced cleavage in single crystals of the nickel-based superalloy PWA 1480E

L9 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Probabilistic distribution of cleavage fracture stress and scatter of fracture toughness

L9 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI On the scattering of the local fracture stress σf*

L9 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Isolated cleavage regions in the ductile fracturing transition of

nuclear-vessel steels and their weld metals

L9 ANSWER 25 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Fractography and characteristics of fracture mechanics in brittle materials

L9 ANSWER 26 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effect of the packet size of tempered martensitic structure on the transition behavior and brittle fracture of steel 2.25Cr-1Mo

L9 ANSWER 27 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI A mechanics-metallurgy approach to cleavage behavior in notched mild steel specimens

L9 ANSWER 28 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Failure of metals and shapes of failed metal surfaces (SCM3)

L9 ANSWER 29 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Reactor surveillance test and fracture mechanics evaluation of irradiation embrittlement in reactor pressure vessel steels

L9 ANSWER 30 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Fracture toughness of denture base acrylics

L9 ANSWER 31 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effect of temperature and notch sharpness on cleavage fracture toughness of high strength steels under impact load

L9 ANSWER 32 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of hydrostatic tension on cleavage fracture of pure polycrystalline zinc

L9 ANSWER 33 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Embrittlement of high-strength steels under high-pressure gaseous hydrogen at room temperature

L9 ANSWER 34 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cleavage fracture in prestrained mild steel

L9 ANSWER 35 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Fracture phenomena in polystyrene

L9 ANSWER 36 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Experimental technique for monitoring dynamic cracks

L9 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Irradiation embrittlement of a low-alloy steel heat treated to different microstructures

L9 ANSWER 38 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Crack and craze propagation in polymers: a fracture-mechanics approach. I. Crack growth in poly(methyl methacrylate) in air

L9 ANSWER 39 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI The effect of microstructure on the cleavage strength of quenched and tempered steels

L9 ANSWER 40 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Direct observation of thermal decomposition produced by fracture in brittle crystalline solid

L9 ANSWER 41 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
TI Fracture of mild steel laminates

L9 ANSWER 42 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN

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TI   Theory and background of fracture mechanics

L9   ANSWER 43 OF 44  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   How to distinguish brittle from tough steel

L9   ANSWER 44 OF 44  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Development of cleavage fractures in mild steels


=> D Hist

     (FILE 'HOME' ENTERED AT 10:03:08 ON 19 MAY 2007)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 10:03:20 ON 19 MAY 2007
L1          1274 S ACTIVATION(5A)NOTCH AND PD<=20040217
L2           503 DUP REM L1 (771 DUPLICATES REMOVED)
L3           524 S CLEAVAGE(5A)NOTCH AND PD<=20040217
L4           253 DUP REM L3 (271 DUPLICATES REMOVED)
L5             6 S MODULATION(S)(CLEAVAGE(5A)NOTCH) AND PD<=20040217
L6             3 DUP REM L5 (3 DUPLICATES REMOVED)
L7            29 S L2 AND L4
L8             2 S L7 AND PD<=19980723
L9            44 S L4 AND PD<=19980723

=> S L9 AND L2
L10            2 L9 AND L2

=> D ibib Abs l10 1-2

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         1999:10383  CAPLUS
DOCUMENT NUMBER:          130:180153
TITLE:                    Ligand-induced cleavage and regulation of nuclear
                          entry of Notch in Drosophila melanogaster embryos
AUTHOR(S):                Kidd, Simon; Lieber, Toby; Young, Michael W.
CORPORATE SOURCE:         Lab. Genetics, The Rockefeller University, New York,
                          NY, 10021-6399, USA
SOURCE:                   Genes & Development (1998), 12(23),
                          3728-3740
                          CODEN: GEDEEP; ISSN: 0890-9369
PUBLISHER:                Cold Spring Harbor Laboratory Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Notch, a transmembrane protein found in a wide range of organisms, is a
     component of a pathway that mediates cell-fate decisions that involve
     intercellular communication.  In this paper, the authors show that in
     Drosophila melanogaster, Notch (N) is processed in a ligand-dependent
     fashion to generate phosphorylated, soluble intracellular derivs.  Suppressor
     of Hairless [Su(H)] is predominantly associated with soluble intracellular N.
     It has been demonstrated by others that N has access to the nucleus, and
     when tethered directly to DNA, the cytoplasmic domain of N can activate
     transcription.  Conversely, a viral activator fused to Su(H) can
     substitute for at least some N functions during embryogenesis.  The
     authors suggest that one function of soluble forms of N is to bind to Su(H),
     and in the nucleus, to act directly as a transcriptional transactivator of
     the latter protein.  Although N has functional nuclear localization
     signals, the N/Su(H) complex accumulates in the cytoplasm and on membranes
     suggesting that its nuclear entry is regulated.  Localization studies in
     cultured cells and embryos suggest that Su(H) plays a role in this
     regulation, with the relative levels of Delta, N and Su(H) determining whether
a
     N/Su(H) complex enters the nucleus.
REFERENCE COUNT:          60    THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:582365 CAPLUS
DOCUMENT NUMBER: 122:320112
TITLE: A study of the brittle fracture characteristics of CoSi2 using laser beam reflections
AUTHOR(S): Anongba, P. N. B.; Oberli, S.; Steinemann, S. G.
CORPORATE SOURCE: Inst. Phys. Experimentale, Univ. Lausanne, Lausanne, CH-1015, Switz.
SOURCE: Acta Metallurgica et Materialia (1995), 43(6), 2275-85
CODEN: AMATEB; ISSN: 0956-7151
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The room temperature brittle fracture characteristics of oriented CoSi2 single crystals with edge notches, subjected to three-point bending expts., have been investigated. A rather uncommon but powerful method has been used: fractured surfaces reflect incident laser beams; the reflected beam pictures correspond to distributions of local surface normals that allow surface elements to be readily characterized. CoSi2 specimens fail according to two distinct mechanisms. The first one corresponds to the fracture of the specimen parallel to a unique crystallog. plane (the notch plane approx.). The directions of fracture propagation are always different from <110>. Various cleavage planes are associated with it such as (101), (111) and some other planes with higher indexes close to (212) and (412). The second mechanism corresponds to the simultaneous activation (about the notch) of various non-parallel local cleavage planes [such as (101), (212), (111) ...] which have the [10.hivin.1] zone axis that corresponds to the direction of fracture propagation. The local cleavage planes have normals located in the (10.hivin.1) plane between [111]-[101] or [101]-[1.hivin.11] or both.

=> D Hist

(FILE 'HOME' ENTERED AT 10:03:08 ON 19 MAY 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 10:03:20 ON 19 MAY 2007
L1 1274 S ACTIVATION(5A)NOTCH AND PD<=20040217
L2 503 DUP REM L1 (771 DUPLICATES REMOVED)
L3 524 S CLEAVAGE(5A)NOTCH AND PD<=20040217
L4 253 DUP REM L3 (271 DUPLICATES REMOVED)
L5 6 S MODULATION(S)(CLEAVAGE(5A)NOTCH) AND PD<=20040217
L6 3 DUP REM L5 (3 DUPLICATES REMOVED)
L7 29 S L2 AND L4
L8 2 S L7 AND PD<=19980723
L9 44 S L4 AND PD<=19980723
L10 2 S L9 AND L2

=> Log off h
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:22:49 ON 19 MAY 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'

AT 10:35:15 ON 19 MAY 2007
FILE 'BIOSIS' ENTERED AT 10:35:15 ON 19 MAY 2007

FILE 'CAPLUS' ENTERED AT 10:35:15 ON 19 MAY 2007

FILE 'EMBASE' ENTERED AT 10:35:15 ON 19 MAY 2007

FILE 'MEDLINE' ENTERED AT 10:35:15 ON 19 MAY 2007

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 83.85 | 84.06 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -4.68 | -4.68 |

=> D Ibib Abs L7 6,8,10,14,17-20,23,25

L7 ANSWER 6 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:165074 BIOSIS
DOCUMENT NUMBER: PREV200400169035
TITLE: Activated forms of notch and methods based thereon.
AUTHOR(S): Artavanis-Tsakonas, Spyridon [Inventor, Reprint Author]; Qi, Huilin [Inventor]; Rand, Matthew D. [Inventor]
CORPORATE SOURCE: Branford, CT, USA
ASSIGNEE: Yale University
PATENT INFORMATION: US 6692919 20040217
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb 17 2004) Vol. 1279, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004
AB The present invention is directed to methods for detecting or measuring Notch activation by observing or measuring the appearance of Notch on the cell surface or by observing or measuring Notch cleavage products that are indicative of Notch activation. The present invention is also directed to methods for detecting a molecule that modulates Notch activation by observing or measuring a change in the amount of Notch expressed on the cell surface or a change in the amount or pattern of Notch cleavage products. The present invention is also directed to a substantially purified activated heterodimeric form of Notch and components thereof and pharmaceutical compositions and kits thereof. The present invention is based, at least in part, on the discovery that Notch in its active form, i.e., the form that mediates signal transduction and that binds Notch ligands such as Delta, is a heterodimer of an about 180 kDa subunit (NEC) and an about 110 kDa subunit (NTM), which are tethered together through a reducing agent-sensitive linkage, in particular, a non-covalent, metal ion-dependent linkage.

L7 ANSWER 8 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:138506 BIOSIS
DOCUMENT NUMBER: PREV200300138506
TITLE: Mind bomb is a ubiquitin ligase that is essential for efficient activation of Notch signaling by Delta.
AUTHOR(S): Itoh, Motoyuki; Kim, Cheol-Hee; Palardy, Gregory; Oda, Takaya; Jiang, Yun-Jin; Maust, Donovan; Yeo, Sang-Yeob; Lorick, Kevin; Wright, Gavin J.; Ariza-McNaughton, Linda; Weissman, Allan M.; Lewis, Julian; Chandrasekharappa, Settara C.; Chitnis, Ajay B. [Reprint Author]

CORPORATE SOURCE: Laboratory of Molecular Genetics, NICHD, NIH, Bethesda, MD, 20892, USA
chitnisa@mail.nih.gov
SOURCE: Developmental Cell, (January 2003) Vol. 4, No. 1, pp. 67-82. print.
ISSN: 1534-5807 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Mar 2003
Last Updated on STN: 12 Mar 2003

AB Lateral inhibition, mediated by Notch signaling, leads to the selection of cells that are permitted to become neurons within domains defined by proneural gene expression. Reduced lateral inhibition in zebrafish mib mutant embryos permits too many neural progenitors to differentiate as neurons. Positional cloning of mib revealed that it is a gene in the Notch pathway that encodes a RING ubiquitin ligase. Mib interacts with the intracellular domain of Delta to promote its ubiquitylation and internalization. Cell transplantation studies suggest that mib function is essential in the signaling cell for efficient activation of Notch in neighboring cells. These observations support a model for Notch activation where the Delta-Notch interaction is followed by endocytosis of Delta and transendocytosis of the Notch extracellular domain by the signaling cell. This facilitates intramembranous cleavage of the remaining Notch receptor, release of the Notch intracellular fragment, and activation of target genes in neighboring cells.

L7 ANSWER 10 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:523260 BIOSIS
DOCUMENT NUMBER: PREV200200523260
TITLE: Activated forms of notch and methods based thereon.
AUTHOR(S): Artavanis-Tsakonas, Spyridon [Inventor]; Qi, Huilin [Inventor, Reprint author]
CORPORATE SOURCE: Branford, CT, USA
ASSIGNEE: Yale University
PATENT INFORMATION: US 6436650 20020820
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 20, 2002) Vol. 1261, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

AB The present invention is directed to methods for detecting or measuring Notch activation by observing or measuring the appearance of Notch on the cell surface or by observing or measuring Notch cleavage products that are indicative of Notch activation. The present invention is also directed to methods for detecting a molecule that modulates Notch activation by observing or measuring a change in the amount of Notch expressed on the cell surface or a change in the amount or pattern of Notch cleavage products. The present invention is also directed to a substantially purified activated heterodimeric form of Notch and components thereof and pharmaceutical compositions and kits thereof. The present invention is based, at least in part, on the discovery that Notch in its active form, i.e., the form that mediates signal transduction and that binds Notch ligands such as Delta, is a heterodimer of an about 180 kDa subunit (NEC) and an about 110 kDa subunit (NTM), which are tethered together through a reducing agent-sensitive linkage.

L7 ANSWER 14 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:547445 BIOSIS
DOCUMENT NUMBER: PREV200100547445
TITLE: GSK3beta phosphorylates Notch and modulates signaling.
AUTHOR(S): Foltz, D. R. [Reprint author]; Nye, J. S. [Reprint author]
CORPORATE SOURCE: Molec. Pharmacol. and Pediatrics, Northwestern Univ., Chicago, IL, USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1443. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002

AB Activation of the Notch signal transduction cascade affects both cell fate in the nervous system as well as the elaboration of neuritic processes. Initiation of the Notch signal transduction cascade by ligand binding results in the intramembraneous cleavage of the Notch protein and release of an intracellular domain (NotchIC) that is able to translocate to the nucleus to initiate transcription of target genes. Phosphorylation of NotchIC proteins has been reported. To uncover the role of phosphorylation in Notch signal transduction, we studied 32p (orthophosphate) incorporation into expressed Notch1 proteins in neuroblastoma cells (N2a). We observed that release of the intracellular domain from the membrane results in an increase in its degree of phosphorylation. Forms of the receptor that harbor mutations that inhibit intramembraneous endoproteolysis do not undergo a hyperphosphorylation, suggesting that phosphorylation of NotchIC occurs only following cleavage. The majority of 32p was incorporated into a region of Notch1 encompassing the downstream nuclear localization signal sequence. This region contains consensus sites for Glycogen Synthase Kinase 3beta (GSK3beta), and we observed that GSK3beta is able to phosphorylate NotchIC both in vitro and in vivo. Inhibition of endogenous GSK3beta or overexpression of a constitutively active form of GSK3beta alters the stability of NotchIC. Finally, GSK3beta null embryonic fibroblasts show a higher degree of HES-1 luciferase reporter activation by NotchIC compared to wild-type, suggesting that GSK3beta acts to inhibit Notch signaling. These data are consistent with a model where Notch signal transduction is modulated by GSK-3beta phosphorylation and destabilization of its intracellular domain.

L7 ANSWER 17 OF 29 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:154757 BIOSIS
DOCUMENT NUMBER: PREV200000154757
TITLE: Calcium depletion dissociates and activates heterodimeric notch receptors.
AUTHOR(S): Rand, Matthew D.; Grimm, Lisa M.; Artavanis-Tsakonas, Spyros; Patriub, Vytas; Blacklow, Stephen C.; Sklar, Jeffrey; Aster, Jon C. [Reprint author]
CORPORATE SOURCE: Division of Molecular Oncology, Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis St., Boston, MA, 02115, USA
SOURCE: Molecular and Cellular Biology, (March, 2000) Vol. 20, No. 5, pp. 1825-1835. print.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Apr 2000
Last Updated on STN: 4 Jan 2002

AB Notch receptors participate in a highly conserved signaling pathway that regulates morphogenesis in multicellular animals. Maturation of

Notch receptors requires the proteolytic cleavage of a single precursor polypeptide to produce a heterodimer composed of a ligand-binding extracellular domain (NEC) and a single-pass transmembrane signaling domain (NTM). Notch signaling has been correlated with additional ligand-induced proteolytic cleavages, as well as with nuclear translocation of the intracellular portion of NTM (NICD). In the current work, we show that the NEC and NTM subunits of Drosophila Notch and human Notch1 (hN1) interact noncovalently. NEC-NTM interaction was disrupted by 0.1% sodium dodecyl sulfate or divalent cation chelators such as EDTA, and stabilized by millimolar Ca2+. Deletion of the Ca2+-binding Lin12-Notch (LN) repeats from the NEC subunit resulted in spontaneous shedding of NEC into conditioned medium, implying that the LN repeats are important in maintaining the interaction of NEC and NTM. The functional consequences of EDTA-induced NEC dissociation were studied by using hN1-expressing NIH 3T3 cells. Treatment of these cells for 10 to 15 min with 0.5 to 10 mM EDTA resulted in the rapid shedding of NEC, the transient appearance of a polypeptide of the expected size of NICD, increased intranuclear anti-Notch1 staining, and the transient activation of an Notch-sensitive reporter gene. EDTA treatment of HeLa cells expressing endogenous Notch1 also stimulated reporter gene activity to a degree equivalent to that resulting from exposure of the cells to the ligand Delta1. These findings indicate that receptor activation can occur as a consequence of NEC dissociation, which relieves inhibition of the intrinsically active NTM subunit.

L7 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1084160 CAPLUS
DOCUMENT NUMBER: 143:419332
TITLE: Notch signaling pathway and its regulation
AUTHOR(S): Hong, Qihua
CORPORATE SOURCE: College of Animal Sciences, Zhejiang University, Hangzhou, 310029, Peop. Rep. China
SOURCE: Xibao Shengwuxue Zazhi (2004), 26(4), 367-371
CODEN: XISZD3; ISSN: 0253-9977
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 36 refs. on Notch signaling pathway and its regulation the Notch receptor, Notch signaling pathway and its regulation at different levels. The Notch receptor is an evolutionarily conserved single-span transmembrane protein family and plays key roles in a wide variety of cell fate decisions during development of both invertebrate and vertebrate species. An intriguing pathway of Notch signaling has been elucidated involving three-step proteolytic cleavages leading to activation of Notch. A number of mols. related and in vivo events have been identified to regulate Notch signaling. Regulation occurs at multiple levels including Notch-ligand interactions, trafficking of receptor and ligands, the cleavage of Notch intracellular, degradation of proteins by ubiquitination, and so on.

L7 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53894 CAPLUS
DOCUMENT NUMBER: 142:235204
TITLE: Notch subunit heterodimerization and prevention of ligand-independent proteolytic activation depend, respectively, on a novel domain and the LNR repeats
AUTHOR(S): Sanchez-Irizarry, Cheryll; Carpenter, Andrea C.; Weng, Andrew P.; Pear, Warren S.; Aster, Jon C.; Blacklow, Stephen C.
CORPORATE SOURCE: Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA
SOURCE: Molecular and Cellular Biology (2004), 24(21), 9265-9273
CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Notch proteins are transmembrane receptors that participate in a highly conserved signaling pathway that regulates morphogenesis in metazoans. Newly synthesized Notch receptors are proteolytically cleaved during transit to the cell surface, creating heterodimeric mature receptors comprising noncovalently associated extracellular (NEC) and transmembrane (NTM) subunits. Ligand binding activates Notch by inducing two successive proteolytic cleavages, catalyzed by metalloproteases and gamma-secretase, resp., that permit the intracellular portion of NTM to translocate to the nucleus and activate transcription of target genes. Prior work has shown that the presence of NEC prevents ligand-independent activation of NTM, but the mechanisms involved are poorly understood. Here, we define the roles of two regions at the C-terminal end of NEC that participate in maintaining the integrity of resting Notch receptors through distinct mechanisms. The first region, a hydrophobic, previously uncharacterized portion of NEC, is sufficient to form stable complexes with the extracellular portion of NTM. The second region, consisting of the three Lin12/Notch repeats, is not needed for heterodimerization but acts to protect NTM from ligand-independent cleavage by metalloproteases. Together, these two contiguous regions of NEC impose crucial restraints that prevent premature Notch receptor activation.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1007009 CAPLUS
DOCUMENT NUMBER: 142:33100
TITLE: Distinct roles of EGF repeats for the Notch signaling system
AUTHOR(S): Sakamoto, Kei; Chao, Wang Sheng; Katsube, Ken-ichi; Yamaguchi, Akira
CORPORATE SOURCE: Molecular Pathology, Graduate School of Tokyo Medical and Dental University, Bunkyo-ku, Tokyo, 113-8549, Japan
SOURCE: Experimental Cell Research (2004), Volume Date 2005, 302(2), 281-291
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Notch is a single-pass transmembrane receptor that mediates cell fate choice in various species and developmental contexts. The Notch signal is transduced by its intracellular domain, which acts as a transcriptional activator, and is released from the plasma membrane by proteolytic cleavages. This process is initiated by intercellular association of the epidermal growth factor (EGF) repeats between Notch and the DSL (Delta, Serrate, Lag-2) ligands but the detailed mechanism is yet to be clarified. Here we demonstrate that Notch1 can form homodimers, which is achieved by its EGF motifs. The Notch1 dimer formation increased in response to ligand presentation and HES1 promoter was stimulated, implying that receptor homodimerization is an important initial step in Notch signal transduction. EGF motifs also serve as a protection against proteases, including TNF-α converting enzyme, which prevents Notch1 from ligand-independent activation. Multiple functions of the Notch EGF motifs, such as the prevention of constitutive activation, reciprocal interaction with the ligands and lateral interaction for homodimerization, appear to constitute crucial elements of the Notch signaling system.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:178254 CAPLUS
DOCUMENT NUMBER: 132:290041

TITLE: A ligand-induced extracellular cleavage regulates γ-secretase-like proteolytic activation of notch1
AUTHOR(S): Mumm, Jeffrey S.; Schroeter, Eric H.; Saxena, Meera T.; Griesemer, Adam; Tian, Xiaolin; Pan, D. J.; Ray, William J.; Kopan, Raphael
CORPORATE SOURCE: Neuroscience Program Division of Biology and Biomedical Sciences Department of Molecular Biology and Pharmacology Department of Medicine Division of Dermatology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Molecular Cell (2000), 5(2), 197-206
CODEN: MOCEFL; ISSN: 1097-2765
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB γ-Secretase-like proteolysis at site 3 (S3), within the transmembrane domain, releases the Notch intracellular domain (NICD) and activates CSL-mediated Notch signaling. S3 processing occurs only in response to ligand binding; however, the mol. basis of this regulation is unknown. Here we demonstrate that ligand binding facilitates cleavage at a novel site (S2), within the extracellular juxtamembrane region, which serves to release ectodomain repression of NICD production Cleavage at S2 generates a transient intermediate peptide termed NEXT (Notch extracellular truncation). NEXT accumulates when NICD production is blocked by point mutations or γ-secretase inhibitors or by loss of presenilin 1, and inhibition of NEXT eliminates NICD production Our data demonstrate that S2 cleavage is a ligand-regulated step in the proteolytic cascade leading to Notch activation.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:90517 CAPLUS
DOCUMENT NUMBER: 130:165155
TITLE: Activated forms of Notch and methods for detecting modulators of Notch signal transduction
INVENTOR(S): Artavanis-Tsakonas, Spyridon; Qi, Huilin; Rand, Matthew D.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9904746 | A2 | 19990204 | WO 1998-US15333 | 19980723 <-- |
| WO 9904746 | A3 | 19990415 | | |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 6436650 | B1 | 20020820 | US 1997-899232 | 19970723 <-- |
| AU 9886621 | A | 19990216 | AU 1998-86621 | 19980723 <-- |
| PRIORITY APPLN. INFO.: | | | US 1997-899232 A | 19970723 |
| | | | WO 1998-US15333 W | 19980723 |

AB The present invention is directed to methods for detecting or measuring Notch activation by observing or measuring the appearance of Notch on the cell surface or by observing or measuring Notch cleavage products that are indicative of Notch activation. The present invention is also directed to methods for detecting a mol. that modulates Notch activation by observing or measuring a change in the amount of Notch

expressed on the cell surface or a change in the amount or pattern of Notch cleavage products. The present invention is also directed to a substantially purified activated heterodimeric form of Notch and components thereof and pharmaceutical compns. and kits thereof. The present invention is based, at least in part, on the discovery that Notch in its active form, i.e., the form that mediates signal transduction and that binds Notch ligands such as Delta, is a heterodimer of an about 180 kDa subunit (NEC) and an about 110 kDa subunit (NTM), which are tethered together through a reducing agent-sensitive linkage, in particular, a non-covalent, metal ion-dependent linkage.

=> D IBib Abs L9 1-5, 9

L9 ANSWER 1 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:358718 BIOSIS
DOCUMENT NUMBER: PREV199800358718
TITLE: The Notch1 receptor is cleaved constitutively by a furin-like convertase.
AUTHOR(S): Loget, Frederique; Bessia, Christine; Brou, Christel; Lebail, Odile; Jarriault, Sophie; Seidah, Nabil G.; Israel, Alain [Reprint author]
CORPORATE SOURCE: Unite Biol. Mol. l'Expression Genique, Unite de Recherche Associee 1773 Cent. Natl. Recherche Sci. Inst. Pasteur, 25 rue du Dr Roux, 75724 Paris Cedex 15, France
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (July 7, 1998) Vol. 95, No. 14, pp. 8108-8112. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 1998
Last Updated on STN: 27 Aug 1998
AB The Notch receptor, which is involved in numerous cell fate decisions in invertebrates and vertebrates, is synthesized as a 300-kDa precursor molecule (p300). We show here that proteolytic processing of p300 is an essential step in the formation of the biologically active receptor because only the cleaved fragments are present at the cell surface. Our results confirm and extend recent reports indicating that the Notch receptor exists at the plasma membrane as a heterodimeric molecule, but disagree as to the nature of the protease that is responsible for the cleavage that takes place in the extracellular region. We report here that constitutive processing of murine Notch1 involves a furin-like convertase. We show that the calcium ionophore A23187 and the alpha1-antitrypsin variant, alpha 1-PDX, a known inhibitor of furin-like convertases, inhibit p300 processing. When expressed in the furin-deficient Lovo cell line, p300 is not processed. In vitro digestion of a recombinant Notch-derived substrate with purified furin allowed mapping of the processing site to the carboxyl side of the sequence RQRR (amino acids 1651-1654). Mutation of these four amino acids (and of two secondary dibasic furin sites located nearby) completely abolished processing of the Notch1 receptor.

L9 ANSWER 2 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:344202 BIOSIS
DOCUMENT NUMBER: PREV199800344202
TITLE: Indirect evidence for delta-dependent intracellular processing of notch in Drosophila embryos.
AUTHOR(S): Lecourtois, Magalie; Schweisguth, Francois [Reprint author]
CORPORATE SOURCE: Ecole Normale Superieure, CNRS ATIPE URA1857, 46 rue d'Ulm, 75230 Paris Cedex 05, France
SOURCE: Current Biology, (June 18, 1998) Vol. 8, No. 13, pp. 771-774. print.
CODEN: CUBLE2. ISSN: 0960-9822.
DOCUMENT TYPE: Article

LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 1998
Last Updated on STN: 13 Aug 1998

AB Cell-cell signalling mediated by the receptor Notch regulates the differentiation of a wide variety of cell types in invertebrate and vertebrate species (1), but the mechanism of signal transduction following receptor activation is unknown. A recent model proposes that ligand binding induces intracellular processing of Notch (2-4); the processed intracellular form of Notch then translocates to the nucleus and interacts with DNA-bound Suppressor of Hairless (Su(H)), a transcription factor required for target gene expression (5-8). As intracellular processing of endogenous Notch has so far escaped immunodetection (1), we devised a sensitive nuclear-activity assay to monitor indirectly the processing of an engineered Notch in vivo. First, we show that the intracellular domain of Notch, fused to the DNA-binding domain of Gal4, regulated transcription, in a Delta-independent manner. Second, we show that full-length Notch, containing the Gal4 DNA-binding domain inserted 27 amino acids carboxy-terminal to the transmembrane domain, activated transcription in a Delta-dependent manner. These results provide indirect evidence for a ligand-dependent intracellular processing event in vivo, supporting the view that Su(H)-dependent Notch signalling involves intracellular cleavage, and transcriptional regulation by processed Notch.

L9 ANSWER 3 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:433997 BIOSIS
DOCUMENT NUMBER: PREV199799733200
TITLE: Metalloprotease-disintegrins: Links to cell adhesion and cleavage of TNF-alpha and Notch.
AUTHOR(S): Blobel, Carl P.
CORPORATE SOURCE: Cell. Biochem. Biophysics Program, Memorial Sloan-Kettering Cancer Cent., New York, NY 10021, USA
SOURCE: Cell, (1997) Vol. 90, No. 4, pp. 589-592.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1997
Last Updated on STN: 8 Oct 1997

L9 ANSWER 4 OF 44 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:388345 BIOSIS
DOCUMENT NUMBER: PREV199799687548
TITLE: Intracellular cleavage of notch leads to a heterodimeric receptor on the plasma membrane.
AUTHOR(S): Blaumueller, Christine M.; Qi, Huilin; Zagouras, Panayiotis; Artavanis-Tsakonas, Spyros [Reprint author]
CORPORATE SOURCE: Howard Hughes Medical Inst., Dep. Cell Biol., Yale Univ., New Haven, CT 06536-0812, USA
SOURCE: Cell, (1997) Vol. 90, No. 2, pp. 281-291.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1997
Last Updated on STN: 10 Sep 1997

AB Previous models for signal transduction via the Notch pathway have depicted the full-length Notch receptor expressed at the cell surface. We present evidence demonstrating that the Notch receptor on the plasma membrane is cleaved. This cleavage is an evolutionarily conserved, general property of Notch and occurs in the trans-Golgi network as the receptor traffics toward the plasma membrane. Although full-length Notch is detectable in the cell, it does not reach the surface. Cleavage results in a C-terminal fragment, N-TM, that appears to be cleaved N-terminal to the transmembrane domain, and an N-terminal fragment, N-EC, that contains most of the extracellular region. We provide evidence that these fragments are tethered together on the plasma membrane by a link

that is sensitive to reducing conditions, forming a heterodimeric receptor.

L9 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:10383 CAPLUS
DOCUMENT NUMBER: 130:180153
TITLE: Ligand-induced cleavage and regulation of nuclear entry of Notch in Drosophila melanogaster embryos
AUTHOR(S): Kidd, Simon; Lieber, Toby; Young, Michael W.
CORPORATE SOURCE: Lab. Genetics, The Rockefeller University, New York, NY, 10021-6399, USA
SOURCE: Genes & Development (1998), 12(23), 3728-3740
CODEN: GEDEEP; ISSN: 0890-9369
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Notch, a transmembrane protein found in a wide range of organisms, is a component of a pathway that mediates cell-fate decisions that involve intercellular communication. In this paper, the authors show that in Drosophila melanogaster, Notch (N) is processed in a ligand-dependent fashion to generate phosphorylated, soluble intracellular derivs. Suppressor of Hairless [Su(H)] is predominantly associated with soluble intracellular N. It has been demonstrated by others that N has access to the nucleus, and when tethered directly to DNA, the cytoplasmic domain of N can activate transcription. Conversely, a viral activator fused to Su(H) can substitute for at least some N functions during embryogenesis. The authors suggest that one function of soluble forms of N is to bind to Su(H), and in the nucleus, to act directly as a transcriptional transactivator of the latter protein. Although N has functional nuclear localization signals, the N/Su(H) complex accumulates in the cytoplasm and on membranes suggesting that its nuclear entry is regulated. Localization studies in cultured cells and embryos suggest that Su(H) plays a role in this regulation, with the relative levels of Delta, N and Su(H) determining whether a N/Su(H) complex enters the nucleus.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:163669 CAPLUS
DOCUMENT NUMBER: 128:214970
TITLE: Kuz family of metalloproteases involved in Notch cleavage and neurogenesis
INVENTOR(S): Rubin, Gerald M.; Pan, Duojia; Rooke, Jenny; Yavari, Reza; Xu, Tian
PATENT ASSIGNEE(S): Regents of the University of California, USA; Yale University
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9808933 | A1 | 19980305 | WO 1997-US15099 | 19970827 <-- |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

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     AU 723836             B2    20000907
     US 5935792            A     19990810    US 1997-937931         19970827 <--
     EP 963432             A1    19991215    EP 1997-939597         19970827 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2000517185         T     20001226    JP 1998-511886         19970827 <--
     CA 2263883            C     20030708    CA 1997-2263883        19970827 <--
     CA 2263883            A1    19980305
     US 6190876            B1    20010220    US 1999-285502         19990402 <--
     US 6319704            B1    20011120    US 2000-709126         20001108 <--
     US 6399350            B1    20020604    US 2001-871385         20010531 <--
     US 2002127621         A1    20020912    US 2001-871388         20010531 <--
PRIORITY APPLN. INFO.:                       US 1996-19390P      P  19960829
                                             US 1997-53476P      P  19970723
                                             US 1997-937931      A3 19970827
                                             WO 1997-US15099     W  19970827
                                             US 1999-285502      A3 19990402
                                             US 2000-709126      A3 20001108
AB   Members of a novel family of polypeptides, the KUZ family, are
     metalloproteases involved in neuronal partitioning and neuronal
     development.  Members of the KUZ family proteins were characterized by
     cDNA cloning from Drosophila, human (transmembrane and soluble forms), mouse,
     and Xenopus.  The full-length Drosophila KUZ cDNA contains an open reading
     frame that encodes a 1239-amino acid membrane-spanning protein of the
     metalloprotease-disintegrin family known as the ADAM family.  Various
     engineered forms of native KUZ proteins lacking protease activity
     interfere with endogenous KUZ activity and function as dominant negatives
     and that dominant negatives can perturb lateral inhibition during
     neurogenesis and result in the overprodn. of primary neurons.  Proteolytic
     processing of NOTCH in embryos to generate the 100-kDa species fails to
     occur in the kuz mutant embryo and expression of dominant negatives in
     imaginal disks or tissue culture cells blocks NOTCH processing.  Thus, the
     primary NOTCH translation product is proteolytically cleaved by native KUZ
     proteins as part of the normal biosynthesis of a functional NOTCH
     receptor.  The invention provides KUZ polypeptides, antibodies that bind
     the KUZ polypeptides, KUZ encoding nucleic acids, methods for identifying
     cells expressing the KUZ polypeptides, methods of identifying ligands that
     bind to the subject proteins and methods of blocking KUZ
     polypeptide/ligand interactions.
REFERENCE COUNT:          7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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 NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29  PHAR reloaded with new search and display fields
 NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26  MEDLINE reloaded with enhancements
 NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16  CASREACT coverage extended
 NEWS 20  MAR 20  MARPAT now updated daily
 NEWS 21  MAR 22  LWPI reloaded
 NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01  New CAS web site launched
 NEWS 29  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS 30  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'MEDLINE' ENTERED AT 15:34:02 ON 19 MAY 2007

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=> S L2 AND heterodimer
L3             0 L2 AND HETERODIMER

=> S L2 and protein
L4           17 L2 AND PROTEIN

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L4   ANSWER 1 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   The ins and outs of Notch signaling.

L4   ANSWER 2 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Notch-related genes in animal development.

L4   ANSWER 3 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   Structure/function studies of lin-12/Notch
     proteins.

L4   ANSWER 4 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   STRUCTURE AND DISTRIBUTION OF THE NOTCH
     PROTEIN IN DEVELOPING DROSOPHILA.

L4   ANSWER 5 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   AMYLOPLAST FROM PARENT NP 113 AND HIGH LYSINE MUTANT NOTCH-2 BARLEY.

L4   ANSWER 6 OF 17  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   NUCLEOTIDE SEQUENCE FROM THE NEUROGENIC LOCUS NOTCH IMPLIES A GENE PRODUCT
     THAT SHARES HOMOLOGY WITH PROTEINS CONTAINING EPIDERMAL GROWTH
     FACTOR-LIKE REPEATS.

L4   ANSWER 7 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   A functional analysis of Notch mutations in Drosophila

L4   ANSWER 8 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   A structural and functional analysis of the Notch protein of
     Drosophila

L4   ANSWER 9 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Intrinsic activity of the lin-12 and Notch intracellular domains in vivo

L4   ANSWER 10 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Specific truncations of Drosophila notch define dominant activated and
     dominant negative forms of the receptor

L4   ANSWER 11 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Xotch, the Xenopus homolog of Drosophila Notch

L4   ANSWER 12 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Structure and distribution of the Notch
     protein in developing Drosophila [Erratum to document cited in
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CA111(19):171398a]

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI A fine structural analysis of the Notch locus in Drosophila melanogaster

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI Molecular genetics of Drosophila neurogenesis

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
TI The Notch locus of Drosophila melanogaster: a molecular analysis

L4 ANSWER 16 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
TI Erratum: Structure and distribution of the Notch protein in developing Drosophila (Genes and Development 3: 1113-1129).

L4 ANSWER 17 OF 17 MEDLINE on STN
TI The expression of the neurogenic locus Notch during the postembryonic development of Drosophila melanogaster and its relationship to mitotic activity.

=> D Ibib Abs L4 1-17

L4 ANSWER 1 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:391486 BIOSIS
DOCUMENT NUMBER: PREV199799690689
TITLE: The ins and outs of Notch signaling.
AUTHOR(S): Weinmaster, Gerry
CORPORATE SOURCE: Biological Chem., Univ. California at Los Angeles Sch. Med., Los Angeles, CA 90095-1737, USA
SOURCE: Molecular and Cellular Neuroscience, (1997) Vol. 9, No. 2, pp. 91-102.
CODEN: MOCNED. ISSN: 1044-7431.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1997
Last Updated on STN: 10 Sep 1997
AB The Notch gene encodes a cell surface protein that regulates cell fate choices in vertebrates and invertebrates. Given the wide variety of cell types influenced by Notch, it would seem that the signal relayed through Notch activation is not an instructive one per se. Rather, Notch signaling is thought to influence the cell's ability to respond to instructive signals responsible for specific cell fates. Expression and functional studies of Notch support this idea; however, the possibility of additional functions for Notch cannot be excluded. Much of what we know about the Notch signaling pathway comes from studies with Drosophila Notch and the Caenorhabditis elegans Notch-related genes lin-12 and glp-1. With the isolation of multiple vertebrate Notch genes we are beginning to understand and define Notch signaling in vertebrates as well. A number of excellent reviews have been published summarizing the current status of Notch/LIN-12/GLP-1 signaling in Drosophila and C. elegans, as well as recent findings with the vertebrate counterparts. Here I review the structure of the various Notch proteins and their putative ligands, and discuss possible interactions between Notch, its ligands, and other cellular components that affect Notch signal transduction. A role for Notch signaling during normal development and in disease processes is discussed in an accompanying review by T. Gridley.

L4 ANSWER 2 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:188698 BIOSIS
DOCUMENT NUMBER: PREV199698744827
TITLE: Notch-related genes in animal development.

AUTHOR(S): Lardelli, Michael; Williams, Reg; Lendahl, Urban [Reprint author]
CORPORATE SOURCE: Lab. Developmental Biol., Dep. Cell Molecular Biol., Karolinska Inst., S-171 77 Stockholm, Sweden
SOURCE: International Journal of Developmental Biology, ( 1995) Vol. 39, No. 5, pp. 769-780.
CODEN: IJDBE5. ISSN: 0214-6282.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 1996
Last Updated on STN: 29 Apr 1996

AB The Drosophila melanogaster gene Notch is central to many cell differentiation events during development. It encodes a large transmembrane signal receptor protein that acts in a poorly understood mechanism of communication affecting the choice of alternative differentiation fates by cells in close proximity. Genes with homology to Notch have been isolated from the nematode Caenorhabditis elegans and a number laboratories, including our own, have isolated multiple vertebrate Notch homologs. In this article we briefly outline the current state of research on Notch and our contribution to it. First, we examine the structure of Notch-related proteins. We then examine the requirements for Notch activity in the development of different organisms and how genetic and transgenic studies are helping us to understand the mechanisms by which these proteins function. We present models for the action of Notch receptors during signal transduction and for the interaction of multiple vertebrate Notch receptors. Finally, we discuss current ideas about the role played by Notch in differentiation and cell-cell communication.

L4 ANSWER 3 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:508564 BIOSIS
DOCUMENT NUMBER: PREV199497521564
TITLE: Structure/function studies of lin-12/ Notch proteins.
AUTHOR(S): Greenwald, Iva
CORPORATE SOURCE: Dep. Biochem. Mol. Biophys., Columbia Univ., Coll. Physicians Surgeons, 701 W. 168th St., New York, NY 10032, USA
SOURCE: Current Opinion in Genetics and Development, (1994 ) Vol. 4, No. 4, pp. 556-562.
ISSN: 0959-437X.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1994
Last Updated on STN: 3 Dec 1994

L4 ANSWER 4 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1989:492514 BIOSIS
DOCUMENT NUMBER: PREV198988119051; BA88:119051
TITLE: STRUCTURE AND DISTRIBUTION OF THE NOTCH PROTEIN IN DEVELOPING DROSOPHILA.
AUTHOR(S): KIDD S [Reprint author]; BAYLIES M K; GASIC G P; YOUNG M W
CORPORATE SOURCE: HOWARD HUGHES MED INST, ROCKEFELLER UNIV, NEW YORK, NY 10021, USA
SOURCE: Genes and Development, (1989) Vol. 3, No. 8, pp. 1113-1129.
CODEN: GEDEEP. ISSN: 0890-9369.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 2 Nov 1989
Last Updated on STN: 4 Nov 1989

AB Antibodies to Notch show that it is a stable, high-molecular-weight transmembrane glycoprotein, with epidermal growth factor (EGF)-like

elements exposed on the cell surface. The protein is phosphorylated variably on serines of the cytoplasmic domain. Individual Notch polypeptide chains appear to be associated with one another by disulfide bonds, suggesting that homotypic interaction of these proteins is required for function. Immunocytochemistry has revealed striking features of Notch expression that might clarify its function: Cells of the ventral neurogenic ectoderm become conspicuously labeled with the protein prior to embryonic neurogenesis, and Notch appears to be associated with cells destined for both neural and epidermal lineages. High levels of Notch become restricted to neuroblasts as they delaminate from the embryonic ectoderm and are apposed to mesoderm. Mesodermal calls express Notch also, suggesting a possible involvement in neurogenesis, or an unknown role in mesoderm differentiation. In larvae and pupae, a correlation of expression and neuroblast mitotic activity is seen for many cells. Notch produced by a dividing neuroblast may persist on derivative cells, including terminally differentiated neurons and nerve processes. In the larval eye imaginal disk, strong Notch expression appears in the morphogenetic furrow, uniformly on cell surfaces as they cluster to form ommatidia. Expression persists on ommatidia after release from the furrow. These patterns suggest a role for Notch in position-dependent development in both initiation and maintenance of cell-surface interactions. In the eye and embryonic ectoderm, uniform expression on cells interacting to produce different developmental lineages from a single primordium suggests that Notch alone may not be sufficient to elaborate cell fates.

L4 ANSWER 5 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1989:181676 BIOSIS
DOCUMENT NUMBER: PREV198987092942; BA87:92942
TITLE: AMYLOPLAST FROM PARENT NP 113 AND HIGH LYSINE MUTANT NOTCH-2 BARLEY.
AUTHOR(S): SANTHA I M [Reprint author]; SWAROOP R; MEHTA S L
CORPORATE SOURCE: DIV OF BIOCHEM, INDIAN AGRIC RES INST, NEW DELHI 110 012
SOURCE: Indian Journal of Biochemistry and Biophysics, (1988) Vol. 25, No. 6, pp. 532-536.
CODEN: IJBBBQ. ISSN: 0301-1208.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 9 Apr 1989
Last Updated on STN: 9 Apr 1989

AB Scanning electron microscopic studies of NP 113 and Notch-2 grains showed differences in structure and shape of starch granules. NP 113 starch had definite oval/bean shape, whereas Notch-2 starch was seen as an aggregated mass between protein and phospholipid. Intact amyloplasts have been isolated from NP 113 and Notch-2 endosperms and their DNA isolated. Restriction pattern of amyloplast DNA showed differences between parent and the mutant. Hybridization with chloroplast specific probes showed homology between the amyloplast DNA and rbc L and psb A genes.

L4 ANSWER 6 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1986:161704 BIOSIS
DOCUMENT NUMBER: PREV198681072120; BA81:72120
TITLE: NUCLEOTIDE SEQUENCE FROM THE NEUROGENIC LOCUS NOTCH IMPLIES A GENE PRODUCT THAT SHARES HOMOLOGY WITH PROTEINS CONTAINING EPIDERMAL GROWTH FACTOR-LIKE REPEATS.
AUTHOR(S): WHARTON K A [Reprint author]; JOHANSEN K M; XU T; ARTAVANIS-TSAKONAS S
CORPORATE SOURCE: DEP OF BIOL, YALE UNIV, KLINE BIOL TOWER, NEW HAVEN, CONN 06520, USA
SOURCE: Cell, (1985) Vol. 43, No. 3 PART 2, pp. 567-582.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA

LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 26 Apr 1986
Last Updated on STN: 26 Apr 1986

AB The primary structure on the Drosophila major embryonic Notch transcript is presented, as determined by sequence analysis of overlapping cDNA clones. The 10,148 bp sequence corresponding to this transcript possesses an 8109 bp open reading frame that potentially codes for a 2703 amino acid protein. We show that this polypeptide contains a repeated structure composed of 36 tandemly arranged 40 amino acid long repeats, which show homology to the epidermal growth factor and other proteins containing EGF-like repeats. Hydropathy plots suggest that the putative Notch protein may span the membrane. We relate these findings to the developmental action of Notch and speculate that the locus may be involved in a cell-cell interaction mechanism that is essential for the differentiation of the ectoderm into neural and epidermal precursors.

L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:592803 CAPLUS
DOCUMENT NUMBER: 127:260420
TITLE: A functional analysis of Notch mutations in Drosophila
AUTHOR(S): Brennan, Keith; Tateson, Richard; Lewis, Karen; Arias, Alfonso Martinez
CORPORATE SOURCE: Department of Zoology, University of Cambridge, Cambridge, CB2 3EJ, UK
SOURCE: Genetics (1997), 147(1), 177-188
CODEN: GENTAE; ISSN: 0016-6731
PUBLISHER: Genetics Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Notch gene encodes a receptor protein that is involved in many processes during development. Its best understood role is during neurogenesis in a process called "lateral inhibition.". However, it has been proposed that Notch also has a role in defining the proneural clusters in the first place. This raises the possibility that the Notch protein is acting as a multifunctional receptor. To test this hypothesis, the authors have carried out a genetic anal. of molecularly characterized Notch alleles to identify alleles that affect only one of the two proposed functions. Here the authors present evidence that Notch alleles can be identified that appear to affect the function of Notch during either lateral inhibition or the definition of proneural clusters. In addition the authors' results indicate that there may be discrete regions of the Notch protein required for each function.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:373177 CAPLUS
DOCUMENT NUMBER: 122:129062
TITLE: A structural and functional analysis of the Notch protein of Drosophila
AUTHOR(S): Rebay, Ilaria
CORPORATE SOURCE: Yale Univ., USA
SOURCE: (1993) 292 pp. Avail.: Univ. Microfilms Int., Order No. DA9418546
From: Diss. Abstr. Int. B, 1994, 55(2), 305
DOCUMENT TYPE: Dissertation
LANGUAGE: English

AB Unavailable

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:577959 CAPLUS
DOCUMENT NUMBER: 119:177959
TITLE: Intrinsic activity of the lin-12 and Notch intracellular domains in vivo

AUTHOR(S): Struhl, Gary; Fitzgerald, Kevin; Greenwald, Iva
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Cell (Cambridge, MA, United States) (1993), 74(2), 331-45
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The lin-12 gene of C. elegans and the Notch gene of D. melanogaster encode structurally related transmembrane proteins that mediate intercellular signaling. The authors show that truncated forms of these proteins consisting of only the intracellular domains cause cell fate transformations associated with constitutive activity in their resp. organisms. This activity does not depend on endogenous gene function. The authors' results indicate that the intracellular domains of Lin-12 and Notch have intrinsic activity and that the principal role of the extracellular domains in the intact proteins is to regulate this activity. The authors' results also suggest that equivalent truncated forms of lin-12/Notch family members in vertebrates, including known oncogenes, are similarly active.

L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:577881 CAPLUS
DOCUMENT NUMBER: 119:177881
TITLE: Specific truncations of Drosophila notch define dominant activated and dominant negative forms of the receptor
AUTHOR(S): Rebay, Ilaria; Fehon, Richard G.; Artavanis-Tsakonas, Spyros
CORPORATE SOURCE: Howard Hughes Med. Inst., Yale Univ., New Haven, CT, 06536-0812, USA
SOURCE: Cell (Cambridge, MA, United States) (1993), 74(2), 319-29
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Notch gene of Drosophila plays an important role in cell fate specification throughout development. To investigate the functions of specific structural domains of the Notch protein in vivo, a series of deletion mutants have been ectopically expressed under the hsp70 heat shock promoter. Two classes of dominant phenotypes are observed, one suggestive of Notch loss-of-function mutations and the other of Notch gain-of-function mutations. Dominant activated phenotypes result from overexpression of a protein lacking most extracellular sequences, while dominant neg. phenotypes result from overexpression of a protein lacking most intracellular sequences. These results support the notion that Notch functions as a receptor whose extracellular domain mediates ligand binding, resulting in the transmission of developmental signals by the cytoplasmic domain. Finally, the phenotypes observed suggest that the cdc10/ankyrin repeat region within the intracellular domain plays an essential role in the postulated signal transduction events.

L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:203863 CAPLUS
DOCUMENT NUMBER: 114:203863
TITLE: Xotch, the Xenopus homolog of Drosophila Notch
AUTHOR(S): Coffman, Clark; Harris, William; Kintner, Chris
CORPORATE SOURCE: Dep. Biol., Univ. California, La Jolla, CA, 92093, USA
SOURCE: Science (Washington, DC, United States) (1990), 249(4975), 1438-41
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mutations of Drosophila and the nematode Caenorhabditis elegans have been

isolated that define a family of related gene products involved in cellular inductions. One of these genes, the Notch gene from Drosophila, is involved with cell fate choices in the neurogenic region of the blastoderm, in the developing nervous system, and in the eye-antennal imaginal disk. The cDNA clones were isolated from Xenopus embryos with Notch DNA to investigate whether cell-cell interactions in vertebrate embryos also depend on Notch-like mols. This approach identified a Xenopus mol., Xotch, which is remarkably similar to Drosophila Notch in both structure and developmental expression.

L4 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:95838 CAPLUS
DOCUMENT NUMBER: 112:95838
TITLE: Structure and distribution of the Notch protein in developing Drosophila [Erratum to document cited in CA111(19):171398a]
AUTHOR(S): Kidd, Simon; Baylies, Mary K.; Gasic, Gregory P.; Young, Michael W.
CORPORATE SOURCE: Howard Hughes Med. Inst., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Genes & Development (1989), 3(12a), 2020
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acknowledgment of the source of the data used for Figure 3a has been provided. The error was not reflected in the abstract or in the index entries.

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:401775 CAPLUS
DOCUMENT NUMBER: 109:1775
TITLE: A fine structural analysis of the Notch locus in Drosophila melanogaster
AUTHOR(S): Wharton, Kristi Anna
CORPORATE SOURCE: Yale Univ., New Haven, CT, USA
SOURCE: (1986) 242 pp. Avail.: Univ. Microfilms Int., Order No. DA8729158
From: Diss. Abstr. Int. B 1988, 48(10), 2882
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:492276 CAPLUS
DOCUMENT NUMBER: 105:92276
TITLE: Molecular genetics of Drosophila neurogenesis
AUTHOR(S): Yedvobnick, B.; Muskavitch, M. A. T.; Wharton, K. A.; Halpern, M. E.; Paul, E.; Grimwade, B. G.; Artavanis-Tsakonas, S.
CORPORATE SOURCE: Dep. Biol., Yale Univ., New Haven, CT, 47405, USA
SOURCE: Cold Spring Harbor Symposia on Quantitative Biology (1985), 50(Mol. Biol. Dev.), 841-54
CODEN: CSHSAZ; ISSN: 0091-7451
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Notch locus of Drosophila salivary gland chromosomes was cloned, and its interactions were studied. The Notch locus was localized within chromosome 3 by chromosome walking and Southern anal., and the phys. map was correlated with the genetic map by studying specific mutations. The Notch locus occurred within 40 kb of DNA at map units -28.5 to +11.3. It directed the synthesis of a 10.5-kb transcript and contained a 93-base-pair-long repetitive sequence (opa) which is found in many developmentally regulated transcripts. Preliminary in situ hybridization showed that the Notch transcripts were not arranged in a tissue-specific

manner in Drosophila embryos. Northern anal. showed that zygotic expression of Notch results in .apprx.2 orders of magnitude higher transcript levels than those found in unfertilized eggs. These data and those of other neurogenic genes are discussed with respect to elucidation, at the mol. level, of the cellular mechanisms involved in neurogenesis.

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:564651 CAPLUS
DOCUMENT NUMBER: 101:164651
TITLE: The Notch locus of Drosophila melanogaster: a molecular analysis
AUTHOR(S): Artavanis-Tsakonas, Spyros; Grimwade, Brian G.; Harrison, Richard G.; Markopoulou, Katerina; Muskavitch, Marc A. T.; Schlesinger-Bryant, Ruth; Wharton, Kristi; Yedvobnick, Barry
CORPORATE SOURCE: Dep. Biol., Yale Univ., New Haven, CT, USA
SOURCE: Developmental Genetics (New York, NY, United States) (1984), 4(4), 233-54
CODEN: DGNTDW; ISSN: 0192-253X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genetic anal. has suggested that neurogenesis in D. melanogaster is under the control of a small number of genes. A mol. study of the genes involved in this developmental event was undertaken, starting with the Notch locus, one of the best characterized loci in terms of its genetic structure and developmental effects. The entire locus is defined by .apprx.40 kb of genomic DNA. The transcriptional activity of these sequences during development has been examined, and an .apprx.10.5-kilobase (kb)-long poly A+ RNA seems essential for wild-type Notch activity. Mapping of this RNA within the phys. map of Notch indicates that it is the processed product of an .apprx.40-kb primary transcription unit spanning the entire Notch locus. More detailed anal. of the 10.5-kb RNA localizes several exons and identifies a small repetitive sequence that seems to be present in the mature Notch transcript. Structural details of a selected number of Notch locus mutations are presented and discussed. Preliminary data on the mol. structure of Notch-homologous DNA sequences in closely related species are also presented.

L4 ANSWER 16 OF 17 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 90023570 EMBASE
DOCUMENT NUMBER: 1990023570
TITLE: Erratum: Structure and distribution of the Notch protein in developing Drosophila (Genes and Development 3: 1113-1129).
AUTHOR: Kidd S.; Baylies M.; Gasic G.P.; Young M.W.
SOURCE: Genes and Development, (1989) Vol. 3, No. 12 A, pp. 2020. .
ISSN: 0890-9369 CODEN: GEDEEP
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L4 ANSWER 17 OF 17 MEDLINE on STN
ACCESSION NUMBER: 89381937 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2506320
TITLE: The expression of the neurogenic locus Notch during the postembryonic development of Drosophila melanogaster and its relationship to mitotic activity.
AUTHOR: Markopoulou K; Artavanis-Tsakonas S
CORPORATE SOURCE: Department of Biology, Yale University, New Haven, CT

06511.
CONTRACT NUMBER: GM29093 (NIGMS)
SOURCE: Journal of neurogenetics, (1989 Sep) Vol. 6, No. 1, pp. 11-26.
Journal code: 8406473. ISSN: 0167-7063.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 26 Oct 1989

AB The molecular analysis of the Notch locus of Drosophila melanogaster demonstrated that it codes for a protein which shows homology to the epidermal growth factor as well as to the products of certain yeast genes involved in the control of the cell cycle (Wharton et al., 1985a; Breeden and Nasmyth, 1987). The structure of the protein suggests that Notch is involved in a cell interaction mechanism which controls the differentiation of several different tissues during development. Here we examine Notch expression during imaginal development using in situ hybridization to tissue sections and demonstrate that Notch is not expressed ubiquitously during the postembryonic stages, but rather is confined to specific tissues. During the larval and early pupal period Notch transcripts are predominantly localized in the imaginal discs and the central nervous system. In the middle and late pupal period the signal levels in these tissues drop dramatically and in the adult animal Notch transcripts are essentially detected only in the ovaries. In the larval stages the pattern of Notch expression appears to be closely correlated with mitotically active tissues, while in later stages this correlation appears less strict. The findings reported here indicate that there is a requirement for normal Notch function in a number of tissues at several developmental stages and that the pleiotropic phenotypic manifestation of Notch mutations is a context dependent developmental result. The observed association of Notch expression with mitotically active cell populations raises the possibility that Notch may play a role in the cell cycle.